REMARKS

Claims 9, 10 and 12-16 have been canceled without prejudice or disclaimer. Claims 1-8, 11 and 17-22 are pending. Applicants respectfully submit that the application is in condition for allowance as set forth below. The present amendment is not a surrender of subject matter and Applicants reserve the right to pursue the original subject matter in a continuing application.

Rejections under 35 U.S.C. §§ 101 and 112, first paragraph

Claims 1-8, 11 and 17-22 were rejected under 35 U.S.C. §§ 101 and 112, first paragraph. According to the Examiner, Claims 1-8, 11 and 17-22 are not supported by a specific and substantial or well-established utility and thus the claims lack utility under 35 U.S.C. § 101 and enablement under § 112, first paragraph. More particularly, the Examiner found that because Applicants do not teach whether the levels of MrgX2 protein (as opposed to MrgX2 mRNA) in the melanoma cells or tissue samples are higher than levels of MrgX2 protein in normal skin tissues, the claimed methods lack utility. Applicants respectfully traverse the rejections.

The claims relate, *inter alia*, to methods of diagnosing skin cancer in a patient involving determining whether cells in a tissue sample from the patient express MrgX2 protein. The Examiner acknowledges that no MrgX2 protein would result in cells lacking MrgX2 mRNA. However, the Examiner alleges that because a level of mRNA expression is not always correlated with the level of its coding protein in the same tissue or cells, the claims lack a specific, substantial utility for diagnosis purposes. Applicants respectfully disagree.

As noted above Claims 1-8, 11 and 17-22 are directed towards methods of diagnosing skin cancer in a patient involving determining whether cells in a tissue sample from the patient express MrgX2 protein. This utility is substantial, i.e. distinguishing cancer cells from normal cells is not an insubstantial or trivial utility without a real world use, and it is specific, i.e. it is directed to a specific disease. Finally, this asserted utility is credible, as one of skill in the art would readily believe that determining expression of a molecule can be used to distinguish tumor tissue from normal tissue.

Applicants respectfully remind the Examiner that Applicants enjoy a presumption that their assertions are true. The Examiner must approach Applicants' assertion of utility as being sufficient to satisfy the utility requirement. M.P.E.P. §2107.02, "Procedural Considerations Related to Rejections for Lack of Utility," states:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope. M.P.E.P.:(2107.02 at III. A., quoting *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (C.C.P.A. 1974) (emphasis in original).

Thus, *In re Langer* and subsequent cases direct the Office to presume that a statement of utility made by an applicant is true ... Office personnel should not begin by questioning the truth of the statement of utility. Instead, any inquiry must start by asking if there is any reason to question the truth of the statement of utility....

Clearly, Office personnel should not begin an evaluation of utility by assuming that an asserted utility is likely to be false, based on the technical field of the invention or for other general reasons. *Id.*

With respect to the use of a method comprising determining whether cells in the tissue sample express MrgX2 with an antibody, the Examiner must accept this assertion as true "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility." Therefore, the question is whether the PTO has established that there is a reason to doubt the objective truth of Applicants' assertion that using standard procedures to examine the expression of MrgX2 in various normal human tissues and melanoma samples, Applicants discovered that MrgX2 mRNA is differentially expressed between normal and tumor tissue such that it can be used in a diagnostic method.

In asserting that Applicants' disclosure of expression of MrgX2 mRNA is insufficient, the Examiner states that Applicants are relying on the fact that "there must be a detectable protein in the cancer tissues if mRNA is detected in said tissues" Office Action at 4. Applicants maintain that, just as desirable pharmaceutical properties in a standard animal model are sufficient to confer utility on a chemical compound because such animal models are generally indicative of results in humans, the demonstration of differential mRNA expression is sufficient to confer utility on a method involving detection of the encoded polypeptide because differential mRNA expression is generally indicative of differential expression of the encoded polypeptide, which renders detection of the polypeptide useful as a diagnostic method. *See, In re Brana*, 34

U.S.P.Q.2d, 1436 (Fed. Cir. 1995). In *In re Brana*, the court found that the PTO's references discussing the predictive value of the animal testing performed by Applicants were not sufficient to show that one skilled in the art would reasonably doubt the asserted utility of the claimed compounds. *Id.* at 1441. Applicants maintain that, just as the PTO was unable to demonstrate a lack of utility by asserting that the animal testing conducted by Applicants in *In re Brana* was insufficiently predictive of the utility, the PTO's assertions regarding the predictive value of a demonstration of differential mRNA expression are insufficient to demonstrate that the claimed methods lack utility. Thus, Applicants continue to maintain that, in view of the general correlation between differential mRNA expression and differential expression of the encoded polypeptides, Applicants' showing of differential expression of the MrgX2 mRNA would lead one skilled in the art to reasonably believe that the MrgX2 polypeptide is differentially expressed, thereby demonstrating the utility of the claimed method.

Applicants note that whether or not an application discloses a utility for a claimed invention is a question of fact. *See, In re Fisher*, 421 F.3d 1365, citing *In re Ziegler*, 992 F.2d 1197 (Fed. Cir. 1993). Any assertion that the claimed invention lacks utility must be supported by substantial evidence. *Id.* at 1369; *In re Gartside*, 203 F.3d 1305 (Fed. Cir. 2000). Applicants respectfully maintain that the Examiner has not provided substantial evidence that the claimed invention lacks utility. In fact, the Examiner's heightened utility requirement is unsupported by any evidence whatsoever. The Examiner provides no evidence or findings of facts to suggest that one skilled in the art would doubt Applicants' disclosed differential expression. Based on the complete failure to present any evidence whatsoever to bring into question Applicants' disclosed differential expression, Applicants submit that the Examiner's heightened requirements for evidence are improper and insufficient to overcome Applicants' presumption of utility.

Moreover, the Examiner's analysis of the utility requirement is flawed. Were the Examiner's analysis correct, the Courts in *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. 881 (C.C.P.A. 1980), *Cross v. Iizuka*, 753 F.2d 1040, 224 U.S.P.Q. 739 (Fed. Cir. 1985), and *Fujikawa v. Wattanasin*, 93 F.3d 1559, 39 U.S.P.Q. 2d 1895 (Fed. Cir. 1996) would have reached a different conclusion. In those cases, there were exceptions to the correlations relied on for the asserted utility. According to the Examiner's analysis, because the *in vitro* screens and preliminary tests in those cases did not always correlate with the asserted utility, one of skill in

the art would have a reason to doubt the asserted utility, and actual direct proof of the asserted utility would be required.

The Examiner's position was rejected by the courts – the courts did not require direct proof of the asserted utility even where there was evidence of exceptions to the general correlation relied on by the applicants: "Of course, it is possible that some compounds active *in vitro* may not be active *in vivo*. But, as our predecessor court in *Nelson* explained, a 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' suffices." *Fujikawa*, 93 F.3d at 1565 (emphasis added).

Claims 1-8, 11 and 17-22 are directed towards methods of diagnosing skin cancer in a patient involving determining whether cells in a tissue sample from the patient express MrgX2 protein. Applicants have established that it is more likely than not that one of skill in the art would believe that because the MrgX2 mRNA is differentially expressed in melanoma tumor tissue compared to normal tissue, the MrgX2 polypeptide will likewise be differentially expressed in skin cancer. Accordingly, when the evidence is applied to the proper standard for utility, it is clear that this differential expression of the MrgX2 polypeptide establishes the claimed methods useful as diagnostic methods for cancer, particularly skin cancer. In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the utility rejection under 35 U.S.C. §101 and the enablement rejection under § 112, first paragraph.

CONCLUSION

For the reasons presented above, Applicants submit that the present application is in condition for allowance and respectfully request the same. If any issues remain, the Examiner is cordially invited to contact Applicants' representative at the number provided below in order to resolve such issues promptly.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: 7-13-07

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